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Title: DEVICE AND METHOD FOR IN-LNE BLOOD TESTING USING BIOCHIPS
Inventor(s): David CHIEN et al.
DOCKET NO.: 072121-0371

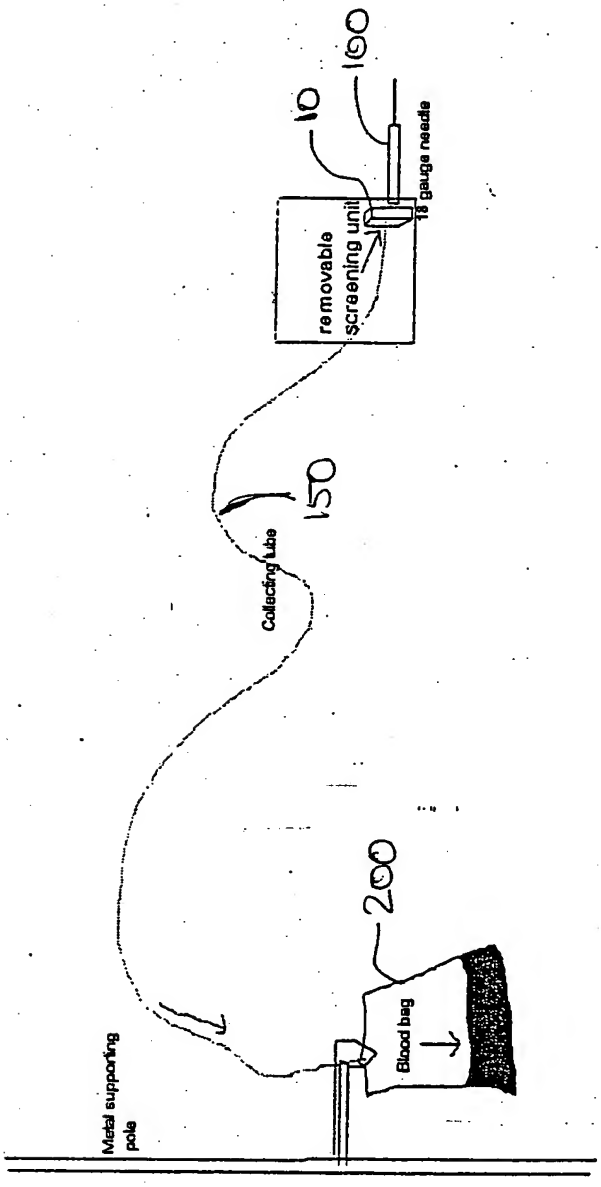

Diagram 1

FIGURE 1A

Title: DEVICE AND METHOD FOR IN-LINE BLOOD TESTING USING BIOCHIPS
Inventor(s): David CHIEN et al.
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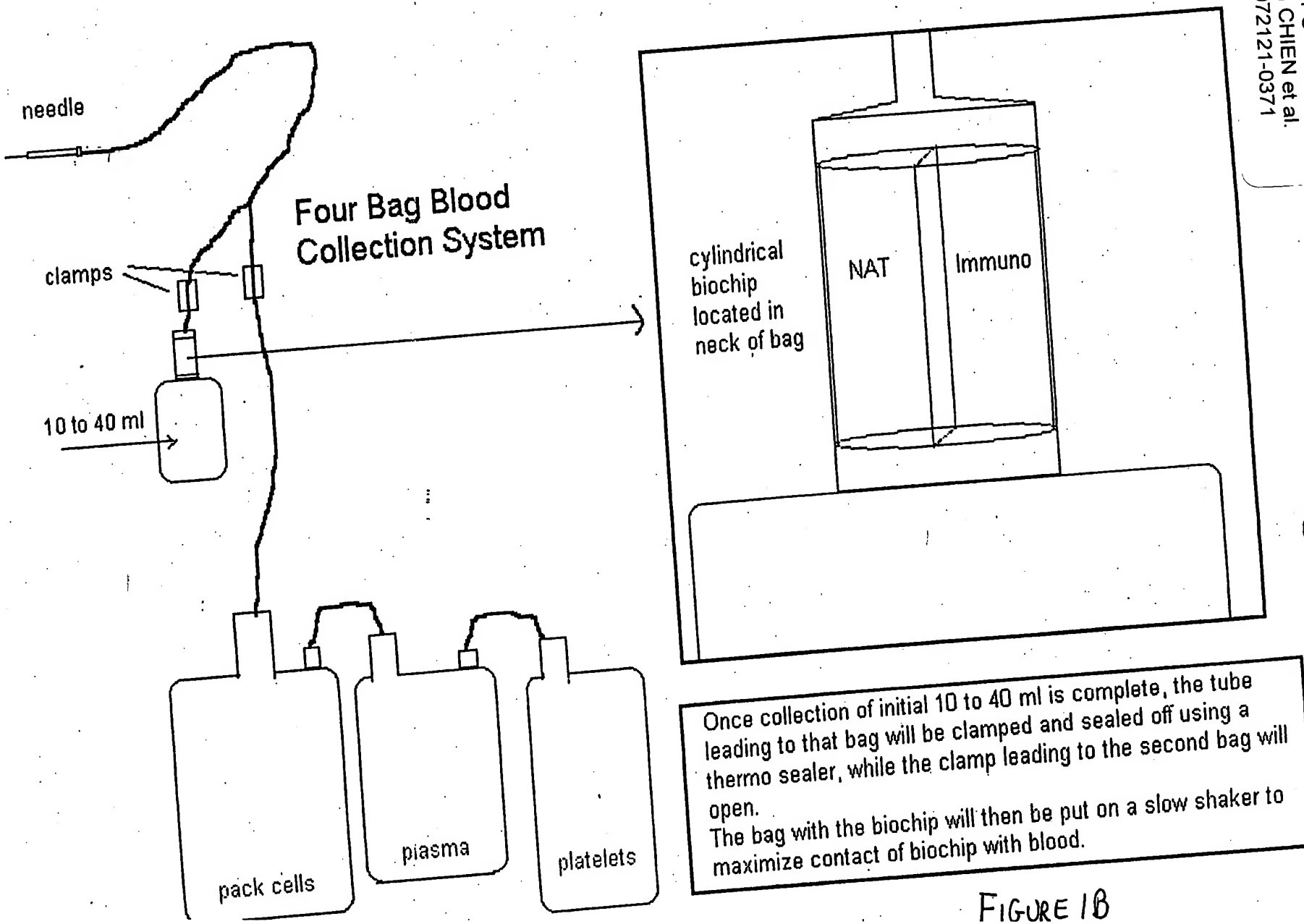

Once collection of initial 10 to 40 ml is complete, the tube leading to that bag will be clamped and sealed off using a thermo sealer, while the clamp leading to the second bag will open.
The bag with the biochip will then be put on a slow shaker to maximize contact of biochip with blood.

FIGURE 1B

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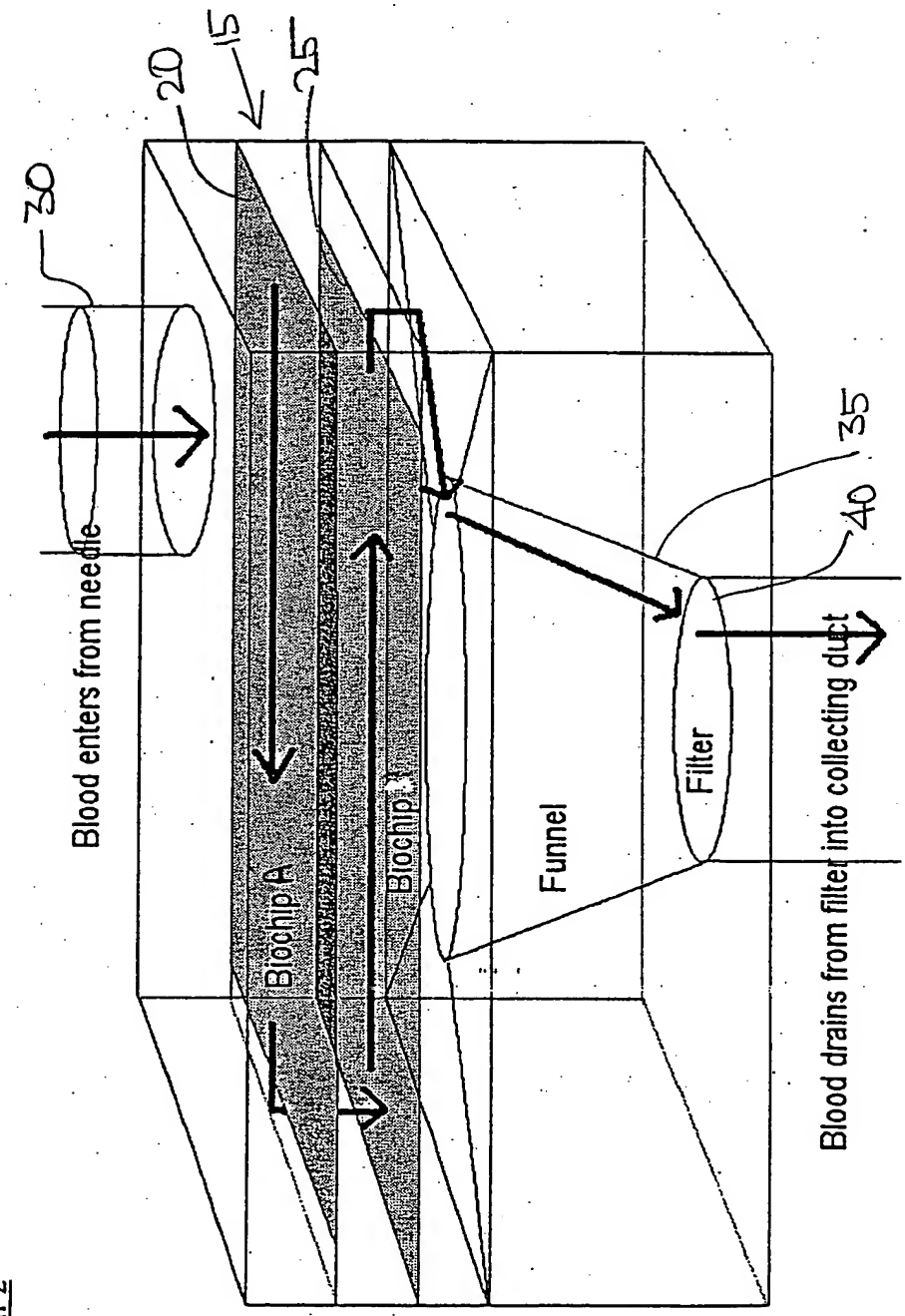


FIGURE 2

Diagram 2

Diagram 3

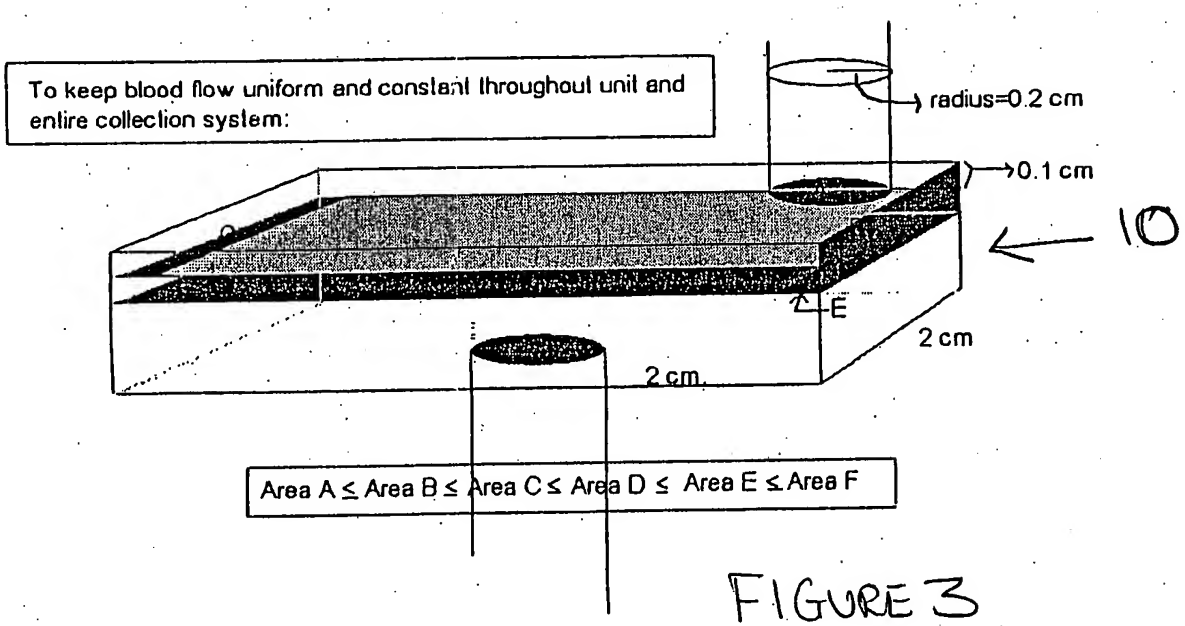


FIGURE 3

Diagram 4

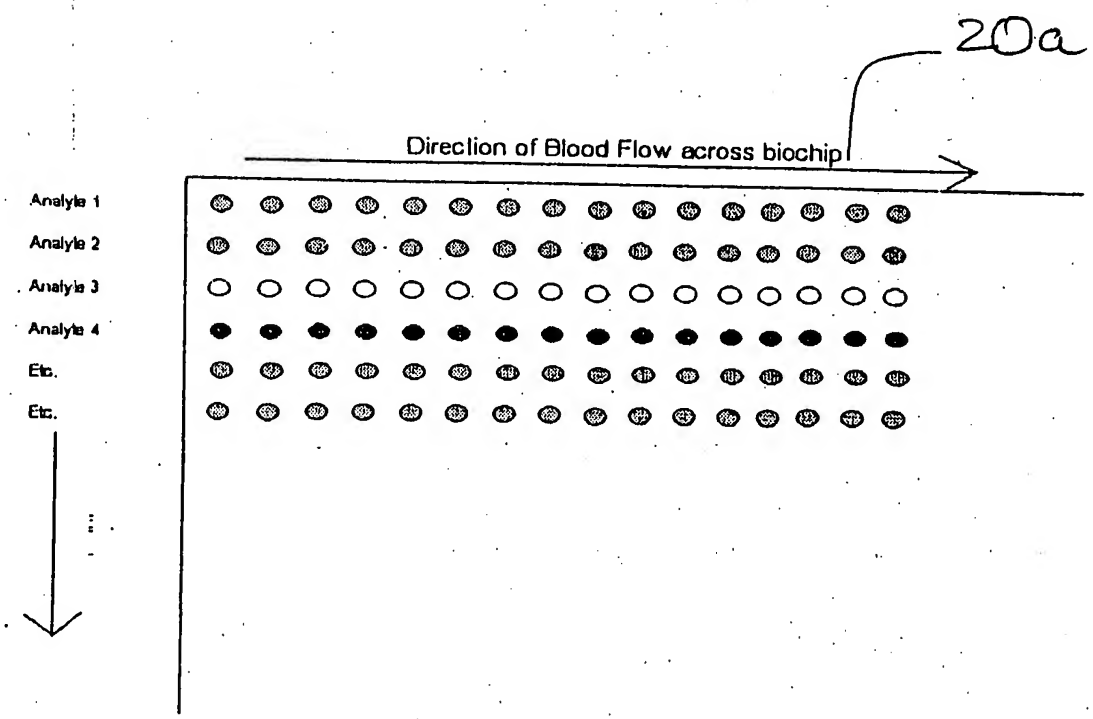
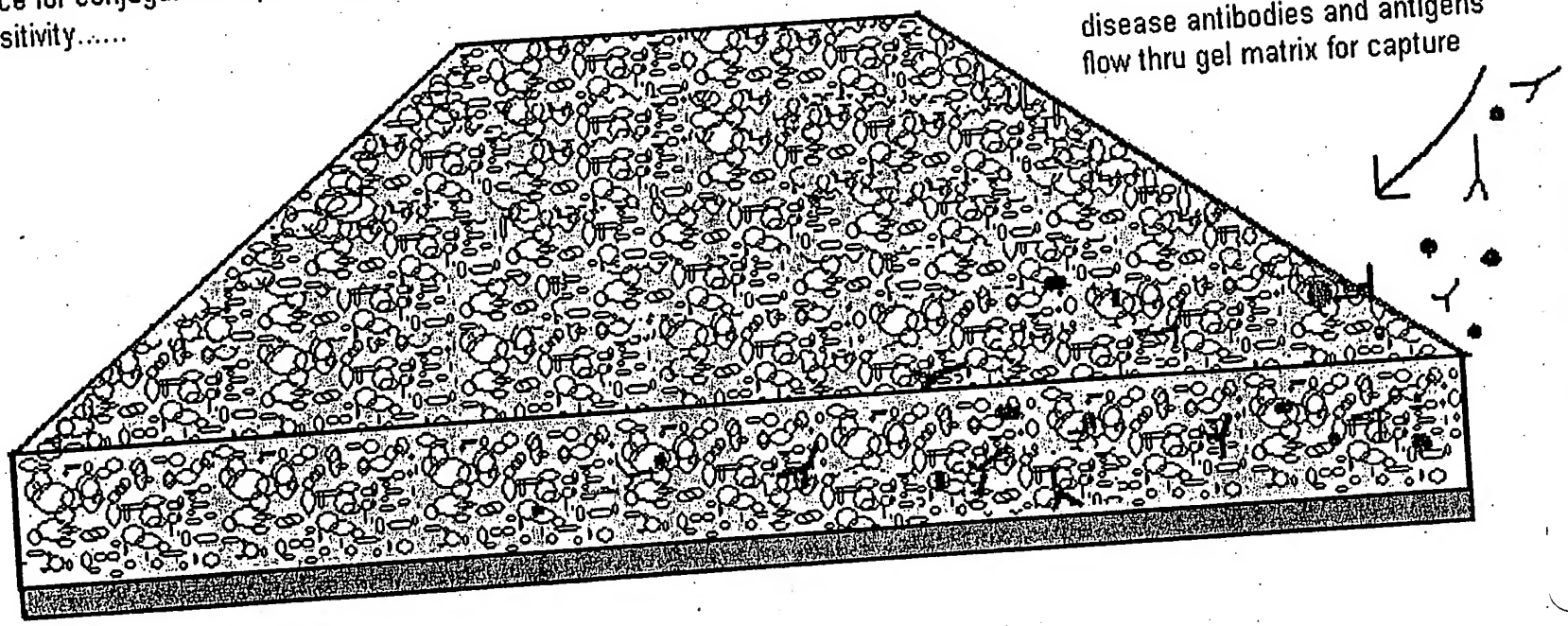


FIGURE 4A

Hypogel technology - 3D matrix to enhance space for conjugation/capture, as well as sensitivity.....



HypoGel® is a hydrophilic polystyrene gel-type resin.
Based on a low crosslinked (1% DVB) polystyrene matrix, oligo ethylene glycols are grafted to form a high loaded hydrophilic resin. The reactive centers are located at the terminus of the glycol spacers. NMR measurements indicate their high flexibility.

FIGURE 4B

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FIG. 4C

Version 2
Entire surface of biochip is rough - no need for wells. The villi-like protrusions will enhance surface area for binding and form a mesh-like surface with submicron-size spaces in-between.

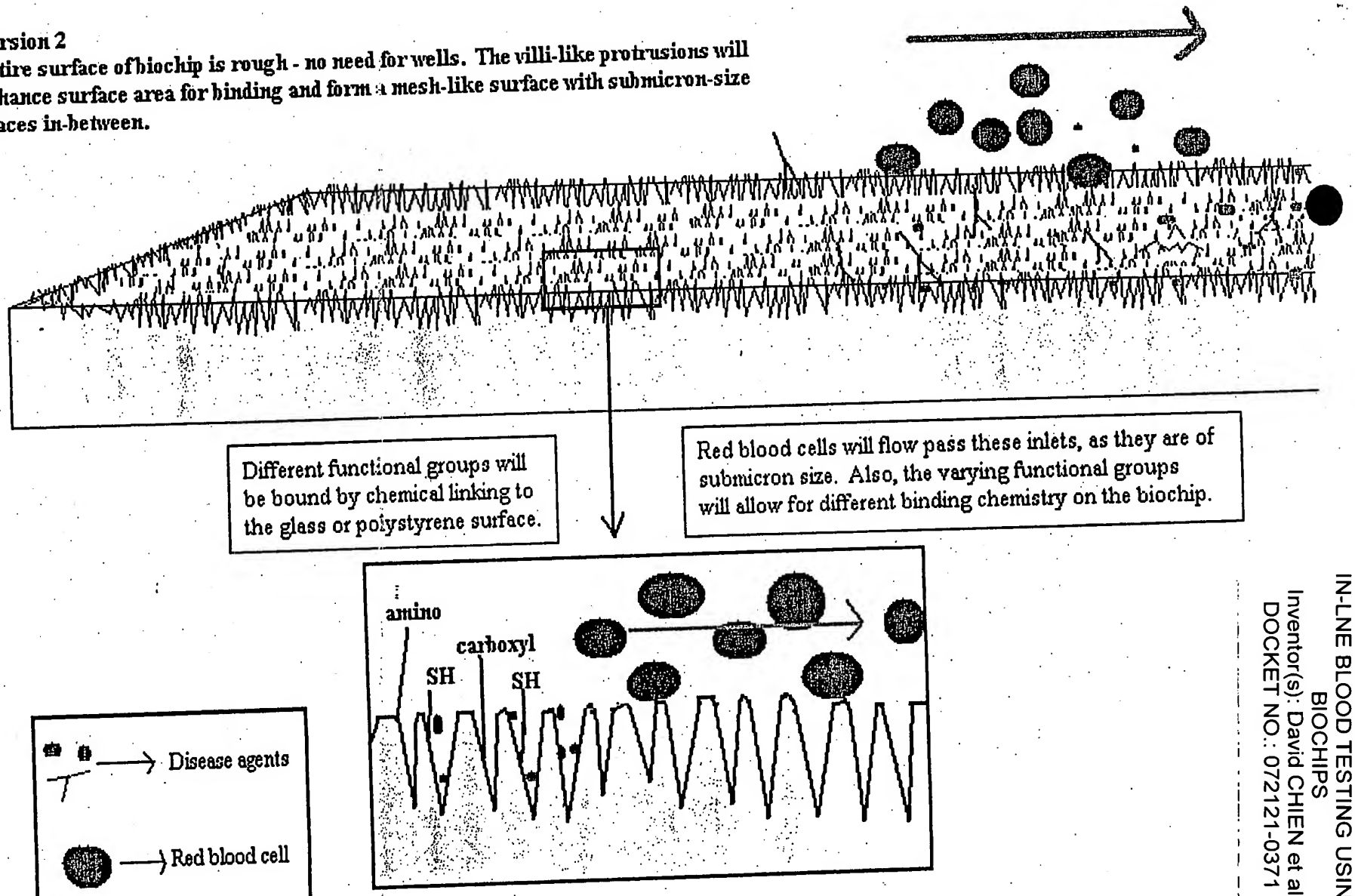

FIG. 4D.

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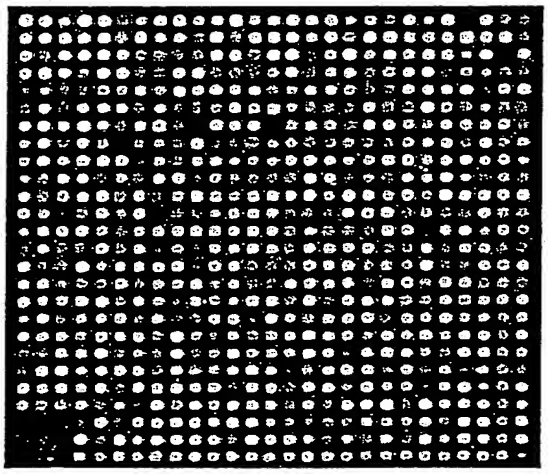
Example of a biochip by Rockefeller University's Gene Array Resource Center (www.rockefeller.edu)



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Analytes to be spotted on Biochip #1 (NAT)

HCV: mAb against core (C22)
mAb against env E1E2
mAb against NS3, NS4, NS5

HIV: mAb against GP120
mAb against P24 core
mAb against P55 core
mAb against P31

HBV: mAb against core
mAb against HBeAg
mAb against HBsAg
mAb against S1 and S2

Also, nucleic acids themselves will be spotted for hybridization:
HCV: 5' end NTR; HIV: LTR region, pol gene region; HBV: preS1/2 and S region

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FIGURE 5

Diagram 5

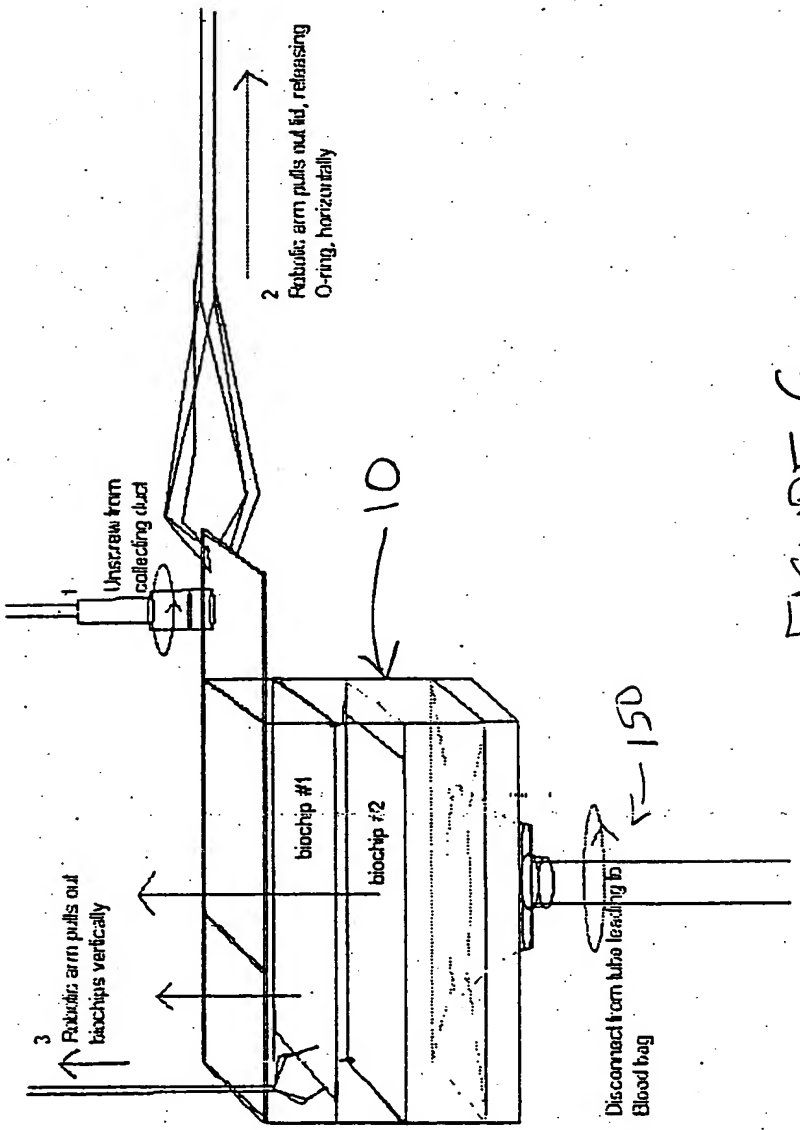

FIGURE 6

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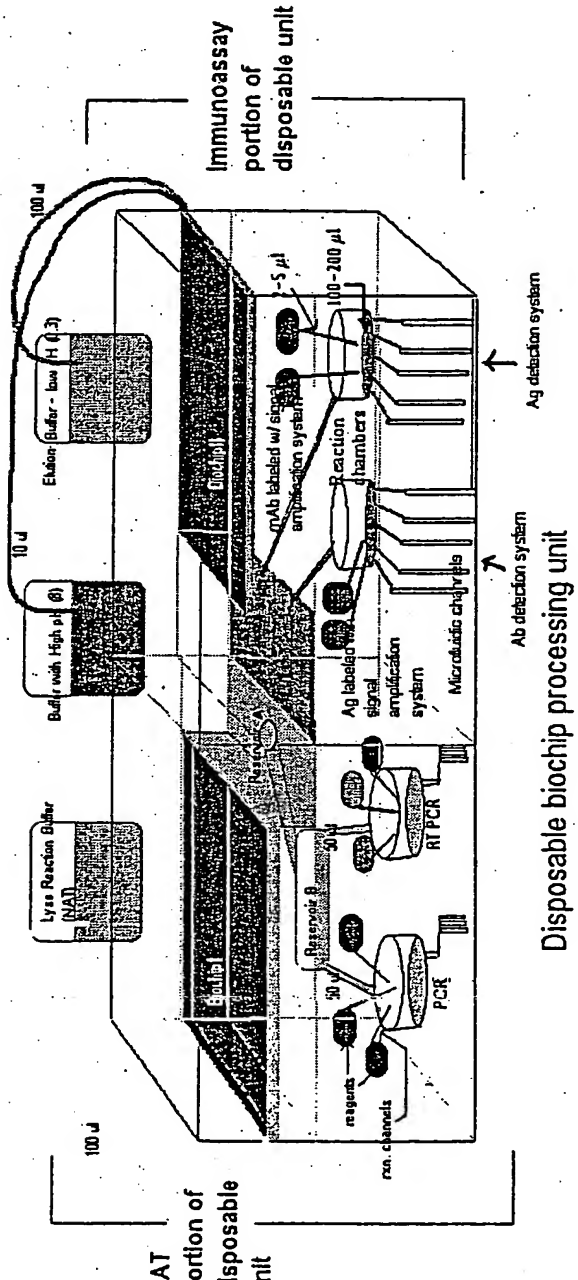

Diagram 6

FIGURE 7A

Alternate design for disposable biochip processor:

Chip *I* and Chip *II* are combined in one. Instead of running reagents for each in parallel, they will run in series, leading ultimately to two separate portions: NAT and Immunoassay.

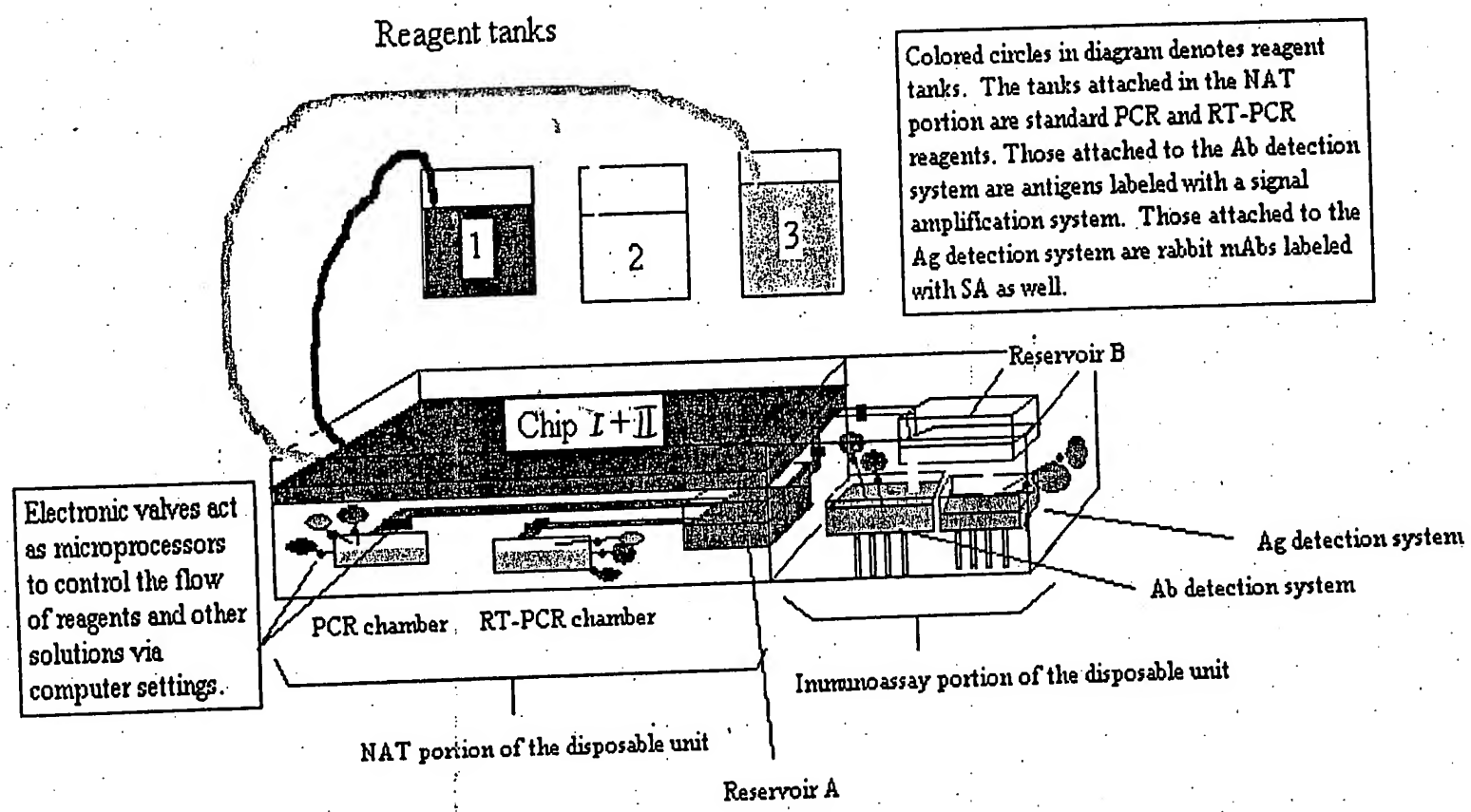

FIGURE 7B

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Diagram 7

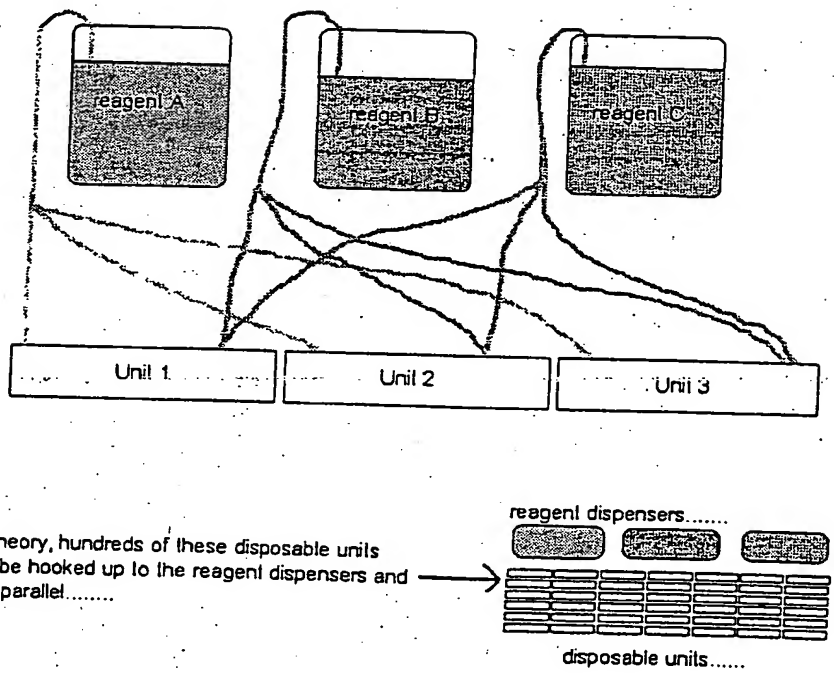


FIGURE 8

Diagram 8

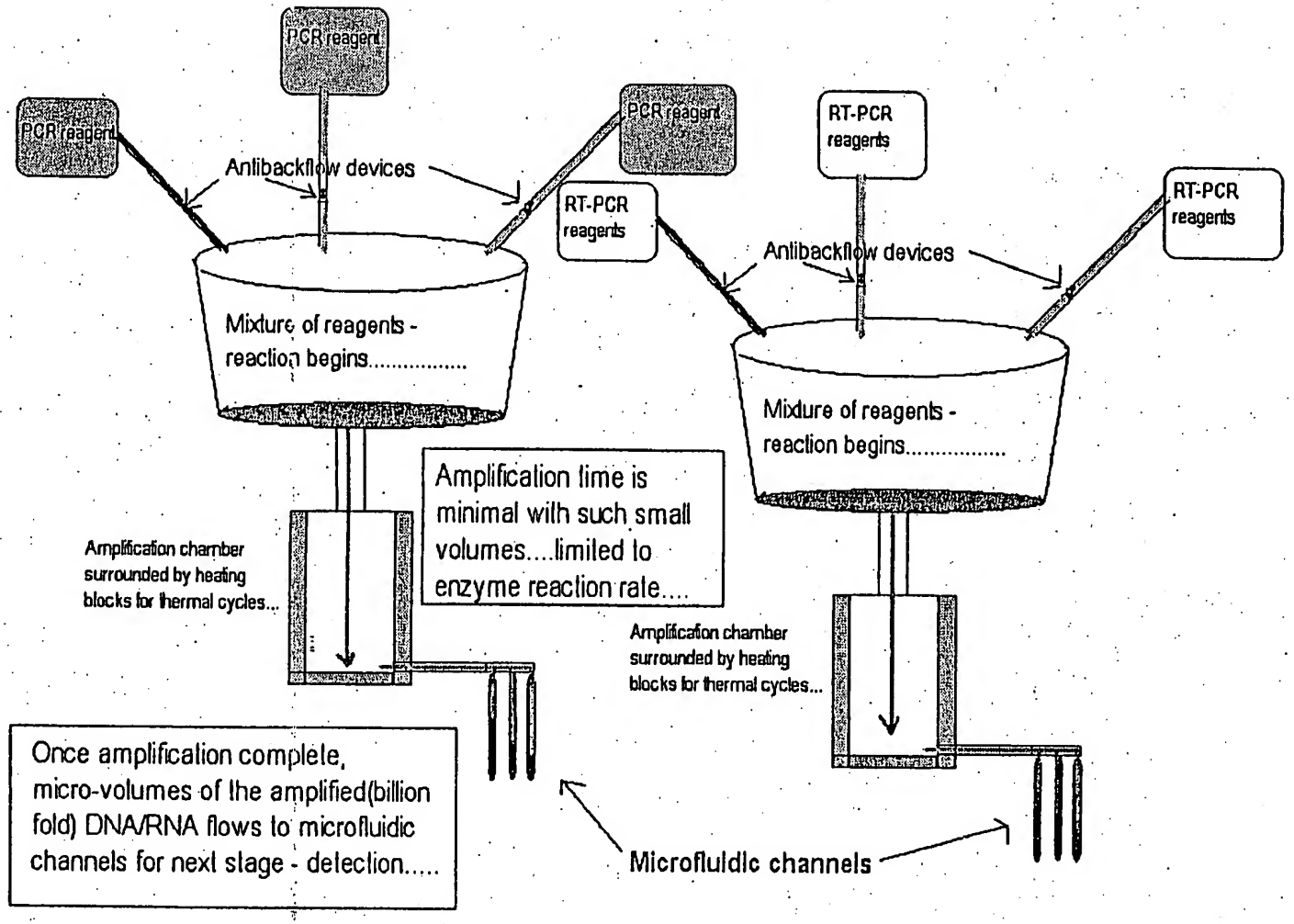


FIGURE 9

Diagram 9

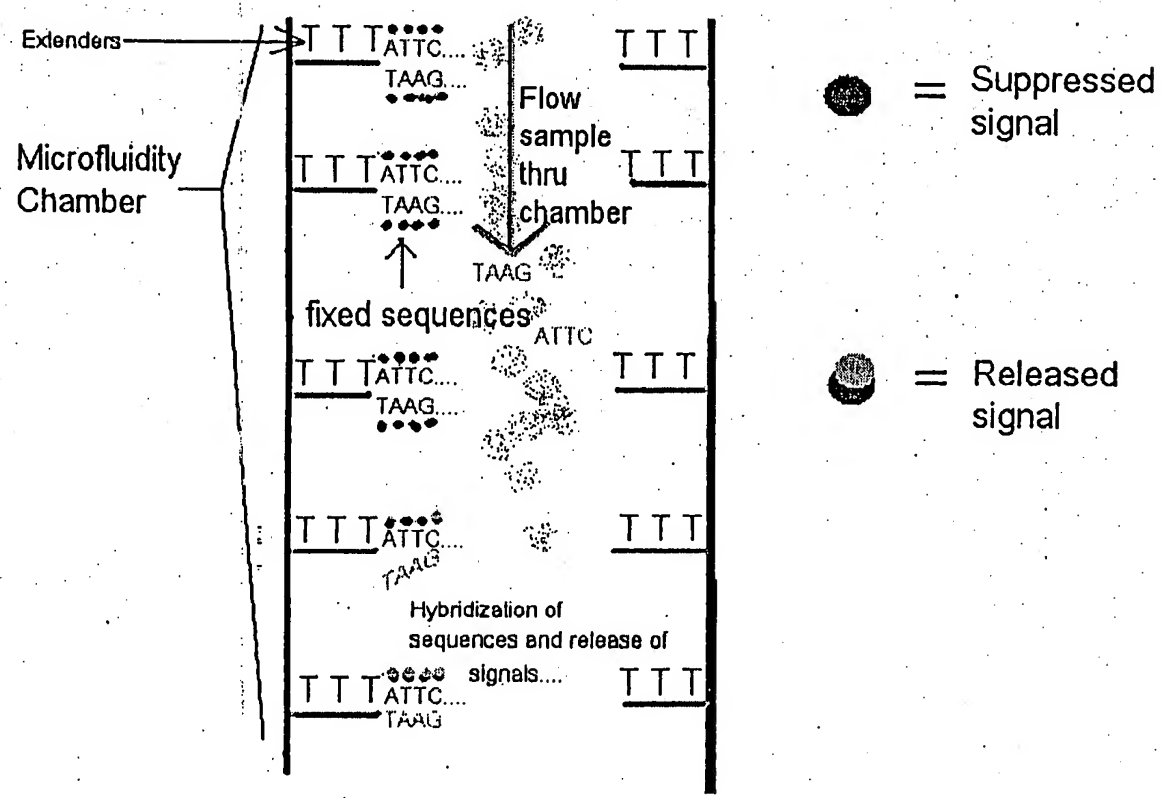


FIGURE 10

Antibody capture and detection:

Version 1

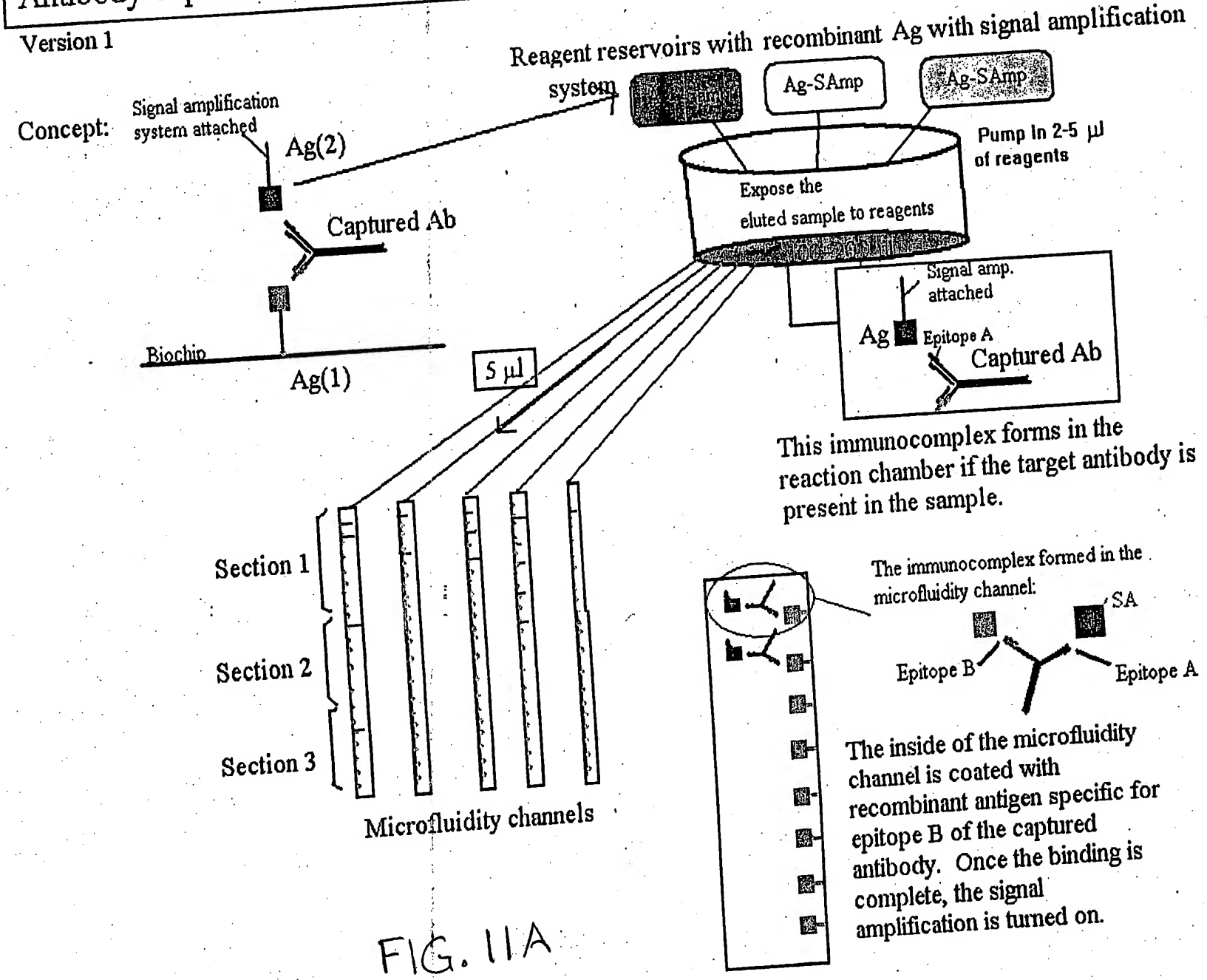


FIG. 11A

Antibody detection
Version 2

The eluted antibodies from the biochip will still be exposed to antigen reagents labeled with signal amplification systems to create an immunocomplex similar to that in Version 1. However.....

Instead of coating the microfluidity channels with recombinant antigen, we would coat them with an excess of anti-human IgG Fc specific for the captured antibody....the human IgG will recognize and bind to the Fc region of the captured antibody.

Immunocomplex formed on channel walls:

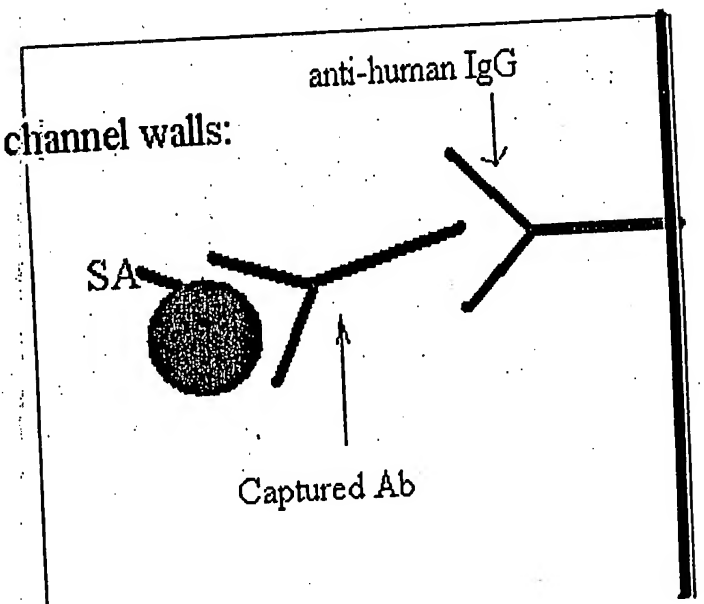


FIG. 11B

Antibody detection
Version 3

Instead of exposing the eluted disease antibodies to a labeled antigen reagent, we will expose them to an anti-human IgG Fc antibody labeled with a signal amplification system. The formed antibody:antibody immunocomplex will then be passed through a microfluidic channel coated with antigen specific to the disease antibodies. In the presence of disease antibodies, the below complex will form and detection is completed via signal amplification.

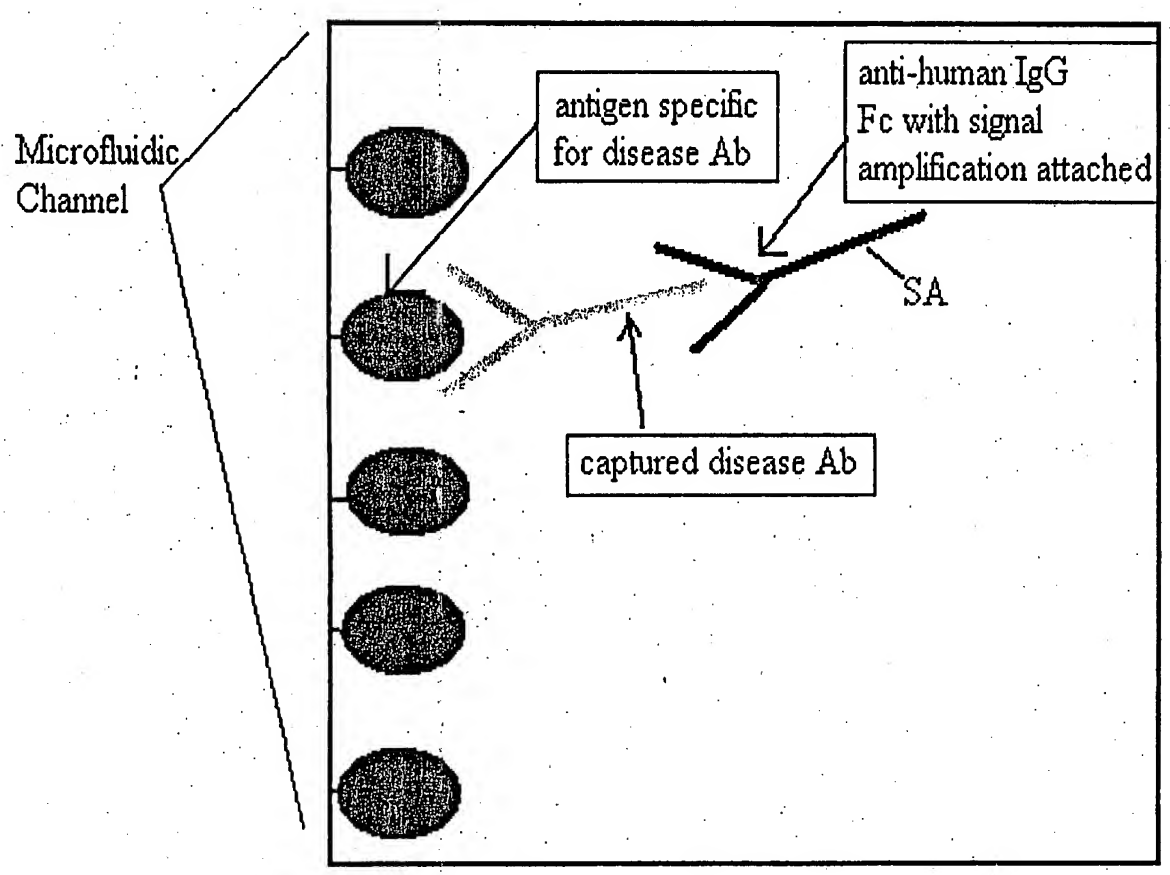
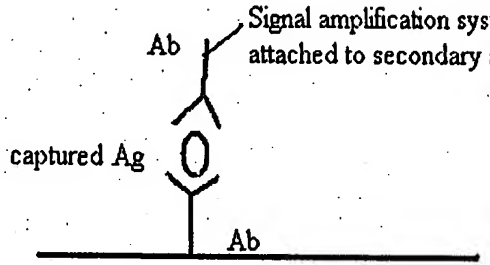


FIG. 11C

Antigen Capture and Detection:

Concept:



Reagent reservoirs with rabbit mAb with signal amplification system

rabbit mAbs with signal amp.

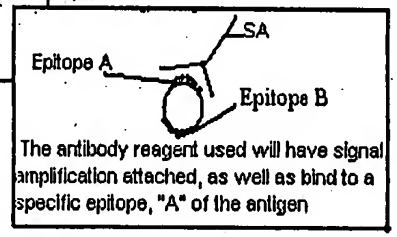
rabbit mAbs with signal amp.

rabbit mAbs with signal amp.

Pump in 2-5 µl of reagents

Expose the eluted sample to reagents

5 µl



The antibody reagent used will have signal amplification attached, as well as bind to a specific epitope, "A" of the antigen

This immunocomplex forms in the reaction chamber if the target antibody is present in the sample.

Section 1

Section 2

Section 3

Microfluidity channels

Mouse mAbs specific to epitope B of the captured antigen are coated on the walls of the microfluidity channels. No false positives

Immunocomplex formed in channel:

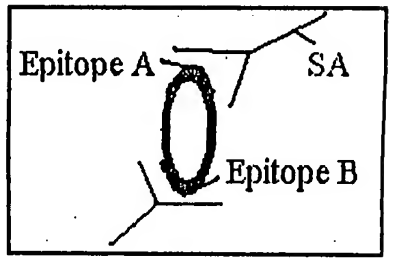


FIGURE 12

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Figure 13: Apparatus for capturing blood pathogen when the blood is flown through:

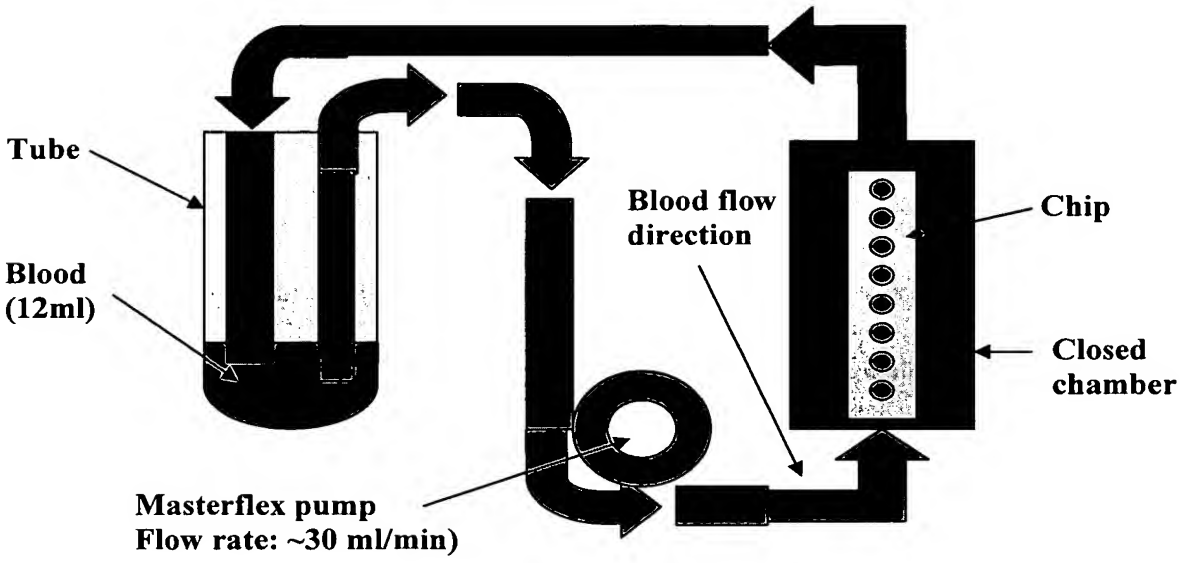

Figure 14: Capture antigen in blood.

In this example, the chip was coated by bovine IgG (A) or monoclonal antibody against HIV P-24 antigen (B). P-24 antigen was added to blood, and was captured by the chip that was coated by monoclonal antibody (B) as shown in the graph, but not by bovine IgG (A).

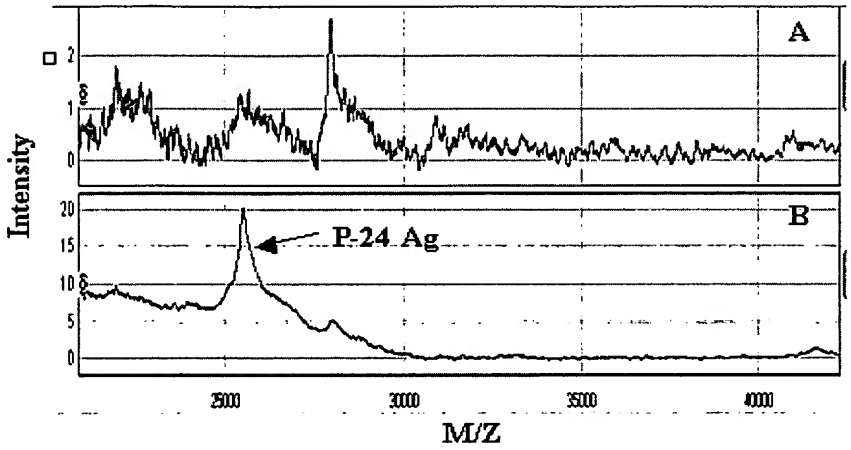

Figure 15: Capture antibody in blood.

In this example, the chip was coated by HIV gp120 envelop protein (A) or HIV P-24 core protein (B). Monoclonal antibody (MonoAb) against P-24 was added to blood, and was captured by the chip that was coated by P-24 antigen (B) as shown in the graph,, but not by gp120 antigen (A).